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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Healthcare Research and Quality

**Scientific Information Request on Core Needle and Open Surgical
Biopsy for Diagnosis of Breast Lesions**

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Scientific Information Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public on core needle and open surgical biopsy for diagnosis of breast lesions. Scientific information is being solicited to inform our review of *Core Needle and Open Surgical Biopsy for Diagnosis of Breast Lesions*, which is currently being conducted by the Evidence-based Practice Centers for the AHRQ Effective Health Care Program. Access to published and unpublished pertinent scientific information on core needle and open surgical biopsy will improve the quality of this review. AHRQ is conducting this comparative effectiveness review pursuant to Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Public Law 108-173, and Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

DATES: *Submission Deadline* on or before **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

ADDRESSES:

Online submissions: <http://effectivehealthcare.AHRQ.gov/index.cfm/submit-scientific-information-packets/>. Please select the study for which you are submitting information from the list to upload your documents.

E-mail submissions: SIPS@epc-src.org.

Print submissions:

Mailing Address:

Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator

PO Box 69539

Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):

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Portland, OR 97239

FOR FURTHER INFORMATION CONTACT:

Robin Paynter, Research Librarian, Telephone: 503-220-8262 ext. 58652
or Email: SIPS@epc-src.org.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Effective Health Care (EHC) Program Evidence-based Practice Centers to complete a review of the evidence for *Core Needle and Open Surgical Biopsy for Diagnosis of Breast Lesions—An Update to the 2009 Report*.

The EHC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on core needle and open surgical biopsy, including those that describe adverse events. The entire research protocol, including the key questions, is also available online at: <http://www.effectivehealthcare.AHRQ.gov/search-for-guides-reviews-and-reports/?pageaction=displayProduct&productID=1723>

This notice is to notify the public that the EHC program would find the following information on core needle and open surgical biopsy helpful:

- A list of completed studies your company has sponsored for this indication. In the list, *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number.*
- *For completed studies that do not have results on ClinicalTrials.gov, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion*

criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies your company has sponsored for this indication.* In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your company for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. The contents of all submissions will be made available to the public upon request. Materials submitted must be publicly available or can be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the Effective Health Care Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EHC program website and available for public comment for a period of 4 weeks. If you would like to be

notified when the draft is posted, please sign up for the e-mail list at:
<http://effectivehealthcare.AHRQ.gov/index.cfm/join-the-email-list1/>.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions. The entire research protocol, is also available online at:

<http://www.effectivehealthcare.AHRQ.gov/search-for-guides-reviews-and-reports/?pageaction=displayProduct&productID=1723>

The Key Questions

The Key Questions (KQs) and study selection criteria (population, intervention, comparator, outcome, timing, and setting; PICOTS) for this update began with those specified in the original report. On the basis of input from clinical experts during the development of this protocol, we have made selected revisions to the KQs and study eligibility criteria to clarify the focus of the updated systematic review.

The following three KQs will be addressed in the review:

Question 1

In women with a palpable or nonpalpable breast abnormality, what is the test performance of different types of core-needle breast biopsy when compared with open biopsy for diagnosis?

- I. What factors associated with the patient and her breast abnormality influence the test performance of different types of core-needle

- breast biopsy when compared with open biopsy for diagnosis of a breast abnormality?
- II. What factors associated with the procedure itself influence the test performance of different types of core-needle breast biopsy when compared with open biopsy for diagnosis of a breast abnormality?
 - III. What clinician and facility factors influence the test performance of core-needle breast biopsy when compared with open biopsy for diagnosis of a breast abnormality?

Question 2

In women with a palpable or nonpalpable breast abnormality, what are the harms associated with different types of core-needle breast biopsy when compared with open biopsy for diagnosis?

- I. What factors associated with the patient and her breast abnormality influence the harms of core-needle breast biopsy when compared with the open biopsy technique in the diagnosis of a breast abnormality?
- II. What factors associated with the procedure itself influence the harms of core-needle breast biopsy when compared with the open biopsy technique in the diagnosis of a breast abnormality?
- III. What clinician and facility factors influence the harms of core-needle breast biopsy when compared with the open biopsy technique in the diagnosis of a breast abnormality?

Question 3

How do open biopsy and various core-needle techniques differ in terms of patient preference, availability, costs, availability of qualified pathologist

interpretations, and other factors that may influence choice of a particular technique?

Study Eligibility Criteria (PICOTS: Population, Intervention, Comparators, Outcomes, Timing, and Setting)

Population

The population for all KQs is women who have been referred for biopsy for the diagnosis of primary breast cancer (including multifocal and bilateral disease) following self-examination, physical examination, or screening mammography. Studies carried out in women at high baseline risk of breast cancer (e.g., due to BRCA mutations) will therefore be included; however studies carried out in women who have been previously diagnosed with breast cancer and are being examined for recurrence will be excluded ^a.

Interventions

For all KQs, the intervention is a core-needle biopsy done to evaluate whether a breast lesion is malignant. Other uses of biopsy techniques (e.g., use of biopsy to examine the sentinel lymph nodes in women with an established diagnosis of breast cancer) are excluded.

Comparators (reference standard and comparator index tests)

For test performance outcomes (KQ 1) the reference standard is either open surgical biopsy or follow-up by clinical examination and/or mammography for at least 6 months. The diagnostic performance of each core biopsy technique (each index test) will be quantified versus the reference standard ^b. The comparative diagnostic performance of alternative core-needle biopsy techniques is also of interest ^c.

For harms and patient-relevant outcomes (outcomes other than diagnostic performance; KQs 2 and 3) the comparators are:

- I. Open surgical biopsy
- II. Follow-up by clinical examination and/or mammography for at least 6 months
- III. Alternative core-needle biopsy methods (e.g., stereotactic mammography vs. ultrasound to locate the breast lesion; use vs. nonuse of vacuum assistance to extract tissue samples)

Outcomes

- I. For KQ 1, test performance outcomes, as assessed by the following measures:
 - A. Sensitivity (proportion of cancerous tumors detected by the reference standard that are also detected by core-needle biopsy)
 - B. False-negative rate (proportion of negative findings according to core-needle biopsy that are classified as positive by the reference standard)
 - C. The underestimation rate for atypical ductal hyperplasia (ADH; proportion of core needle biopsy findings of ADH that are found to be malignant according to the reference standard)
 - D. The underestimation rate for DCIS (proportion of core-needle biopsy findings of DCIS that are found to be invasive according to the reference standard)

- II. For KQ 2:

- A. Rate of inconclusive biopsy findings (e.g., inadequate sampling of the lesion)
- B. Repeat biopsy rate
- C. Subsequent false-positive and false-negative rates on mammography
- D. Dissemination (seeding) of cancerous cells along the needle track
- E. Patient-centered outcomes (including bruising, bleeding or hematomas, pain, use of pain medication, infections, fainting or near fainting, and time to recover)

III. For KQ 3:

- A. Patient-relevant outcomes
 - 1. Patient preferences for specific procedures
 - 2. Cosmetic results
 - 3. Quality of life
 - 4. Anxiety and other psychological outcomes
 - 5. Time to complete tumor removal (for women with cancer)
 - 6. Recurrence rate (for women with cancer, including local, regional, and distant recurrence)
 - 7. Cancer-free survival and overall survival
- B. Resource use and logistics
 - 1. Costs
 - 2. Resource utilization other than cost (number of additional surgical procedures [e.g., re-excisions, procedural time])
 - 3. Subsequent surgical procedures
 - 4. Wait time for test results

C. Availability of technology and relevant expertise

1. Physician experience
2. Availability of equipment
3. Availability of (qualified) pathologists to evaluate biopsy samples

Timing

Duration of clinical and/or mammographic follow-up must be at least 6 months in studies where open surgical biopsy was not performed.

Setting

Studies in all geographic locations and care settings will be evaluated, including general hospitals, academic medical centers, and ambulatory surgical centers, among others.

EXPLANATION TO REFERENCES IN POPULATION AND INTERVENTIONS SECTIONS ABOVE

^a The original review excluded studies carried out in women at high risk of breast cancer; however, magnetic resonance imaging (MRI)-guided biopsy, which has been identified as a topic of interest for the updated review, is used mainly in this subset of patients. For this reason, following extensive discussions with the TEP (Technical Expert Panel), we decided to broaden the scope of the review to cover women at high risk for cancer. In effect, this will be a de novo review with respect to this population subset.

^b Most assessments of diagnostic performance quantify the sensitivity and the specificity of each index test—here each core-needle biopsy technique. Sensitivity and specificity are probabilities conditional on true

disease status and are noncomparative in nature. The reference standard is used in their definition and is not a “comparator test.”

^c That is, differences or ratios of sensitivities and of specificities between alternative core-needle biopsy techniques.

Dated: October 31, 2013

Richard Kronick,
AHRQ Director

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